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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,028	03/22/2004	Robert Karlsson	B 521	1001

22840 7590 12/18/2009

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EXAMINER	
GRUN, JAMES LESLIE	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
12/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/806,028	KARLSSON ET AL.	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,13,17,21,25-29 and 45-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8,13,17,21,25-29 and 45-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08 October 2009 has been entered.

Claims 45-52 are newly added. Claims 2-7, 9-12, 14-16, 18-20, 22-24, and 30-44 have been cancelled. Claims 1, 8, 13, 17, 21, 25-29, and 45-52 remain in the case.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1, 8, 13, 17, 21, and 25-29 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Cooper et al. (Anal. Biochem. 277: 196, 2000), Niemeyer et al. (Anal. Biochem. 268: 54, 1999), and Nikiforov et al. (US 5,610,287) for reasons of record in the prior rejection of the similar subject matter of these claims repeated below for convenience.

Cooper et al. teach sensor chips having 4 flow cells and having modified carboxymethyl dextran hydrogels, to which streptavidin was covalently bound (see e.g. page 203; SA sensor chips), deposited on a gold film for surface plasmon resonance determinations of molecule binding interactions. Biotinylated oligonucleotides in a high salt (1 M NaCl) buffer were bound to the immobilized streptavidin, washed, and used for binding to complementary nucleotides (see e.g. page 198). The reference also teaches layering of biotin and streptavidin for an oligonucleotide immobilization method involving negatively charged vesicles. In contrast to the invention as instantly claimed the reference does not teach cationic detergent solutions for immobilization of biotinylated oligonucleotides.

Niemeyer et al. also teach immobilization of biotinylated oligonucleotides to SA sensor chips or to streptavidin-coated microplate wells for immobilization of other components having complementary nucleotide portions. An immobilization buffer comprising salt was used (see e.g. page 56). In contrast to the invention as instantly claimed the reference does not teach cationic detergent containing compositions for immobilization of biotinylated oligonucleotides.

Nikiforov et al. teach compositions and methods for immobilization of oligonucleotides using the alternatives of cationic detergents or salts. The reference contacted mixtures of cationic detergents, including cetyltrimethylammonium bromide (CTAB) (see e.g. col. 5) or1-ethyl-3-(3'-dimethylaminopropyl)-1,3-carbodiimide hydrochloride (EDC) (see cols. 7-8), with oligonucleotides for immobilization onto negatively-charged solid surfaces by either covalent or non-covalent binding (see e.g. cols. 14-16, Table 3). Different areas of the same solid support (wells in a microtitier plate) were treated similarly or differently. After immobilization, the detergent was washed away, leaving the immobilized oligonucleotides on the surface of the solid

phase. However, the presence of vesicular structures in the mixture of EDC (see cols. 7-8) with oligonucleotides used in the immobilization of the oligonucleotides onto negatively-charged solid surfaces cannot be determined by the examiner.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have substituted compositions comprising cationic detergents for the salt containing solutions used in Cooper et al. or Niemeyer et al. for oligonucleotide immobilization because Nikiforov et al. teach cationic detergent compositions as an alternative to salt containing compositions for oligonucleotide immobilization. One would have had an extremely reasonable expectation of success in using the cationic detergent reagents of Nikiforov et al. in the immobilization methods of Cooper et al. or Niemeyer et al. because Nikiforov et al. had already shown such reagents to be effective for oligonucleotide immobilization and one would have been motivated to have selected from known alternatives to perform the immobilization. Nothing unobvious is seen in the substitution of one known reagent for another to obtain the expected predictable result.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Applicant's arguments filed 08 October 2009 have been fully considered but they are not deemed to be persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re*

Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this regard, and notwithstanding applicant's assertions to the contrary, the disclosure of Nikiforov et al. is not relied upon for any particular mechanism of binding. However, applicant's arguments were not found persuasive because the teachings of the reference are not limited to hydrophobic interaction binding, as argued, because the reference clearly teaches both covalent or non-covalent binding (see e.g. cols. 14-16, Table 3) and that the mechanisms of non-covalent binding are unknown, but may involve decreasing of electrostatic repulsion between the phosphates of the oligonucleotide and the negatively charged groups on the surface allowing a combination of hydrophobic, ionic and hydrogen bonding to the surface (see e.g. col. 7, lines 33-59, and col. 8, lines 63-67). Moreover, for the reasons of record, the references of Cooper et al. or Niemeyer et al. are relied upon for their teachings that salt containing solutions were effective for the immobilization of biotinylated oligonucleotides to the same surface as instantly disclosed and claimed. As set forth, Nikiforov et al. is relied upon for teaching cationic detergent compositions as an alternative to salt containing compositions for oligonucleotide immobilization to negatively charged surfaces, including for biotinylated oligonucleotide immobilization (see e.g. col. 7 and col. 8, lines 58-67). As set forth, one of ordinary skill in the art would have had an extremely reasonable expectation of success in using the cationic detergent reagents of Nikiforov et al. as an alternative in the immobilization methods of Cooper et al. or Niemeyer et al. because Nikiforov et al. had already shown such reagents to be an effective alternative for oligonucleotide immobilization and one would have been motivated to have selected from a limited number of known alternatives to perform the immobilization.

Applicant further urges that Nikiforov et al. teaches against micelles. This is not found persuasive because applicant is arguing a limitation that is no longer claimed and because of the extensive reasons of record.

Claims 45-52 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Pieken et al. (US 7,427,678), Vary (Clin. Chem. 38: 687, 1992), and Nikiforov et al. (US 5,610,287).

Pieken et al. teach a method for immobilization of molecules, such as oligonucleotides, on a support (see e.g. col. 5-6), such as a sensor chip having a modified carboxymethyl dextran hydrogel matrix coating thereon (see e.g. col. 43-44), for use in binding assays (see e.g. col. 46). The rate of the immobilization reaction can be increased by hydrophobic conditions, including the presence of some salts (see e.g. col. 2). The reference teaches the advantages of covalent attachment of oligonucleotides to a surface for use as a probe (see e.g. col. 1) and teaches commonly employed prior covalent immobilization methods (see e.g. col. 1 and cols. 49-50). In contrast to the invention as instantly claimed the reference does not teach detergents for the immobilization.

Vary teaches the covalent immobilization of aminoalkyl derivatives of oligonucleotides to a carboxylated solid phase by stepwise addition of the oligonucleotides and 1-ethyl-3,3-(3-dimethylaminopropyl)-carbodiimide to the solid phase. In contrast to the invention as instantly claimed the reference does not teach a sensor chip having a modified carboxymethyl dextran hydrogel matrix coating thereon or premixing oligonucleotide and the carbodiiimide for the immobilization reaction.

Nikiforov et al. teach compositions and methods for immobilization of oligonucleotides using the alternatives of cationic detergents or salts. The reference contacted mixtures of cationic detergents, including cetyltrimethylammonium bromide (CTAB) (see e.g. col. 5) or 1-ethyl-3-(3'-dimethylaminopropyl)-1,3-carbodiimide hydrochloride (EDC) (see cols. 7-8), with oligonucleotides for immobilization onto negatively-charged solid surfaces. Different areas of the same solid support (wells in a microtitier plate) were treated similarly or differently. After immobilization, the detergent was washed away, leaving the immobilized oligonucleotides on the surface of the solid phase. The mixture of the cationic detergent 1-ethyl-3-(3'-dimethylaminopropyl)-1,3-carbodiimide hydrochloride (EDC) (see cols. 7-8) with oligonucleotides was shown to act not only in the non-covalent binding of oligonucleotides onto negatively-charged solid surfaces but also in the covalent immobilization of oligonucleotides onto negatively-charged solid surfaces comprising carboxylate groups (see e.g. cols. 14-16, Table 3).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have covalently immobilized oligonucleotides to a solid phase, such as a sensor chip having a modified carboxymethyl dextran hydrogel matrix coating thereon, for use in binding assays for the benefits specifically taught by Pieken et al. One would have been motivated to select from the known methods for covalent immobilization of oligonucleotides taught by Pieken et al. and/or Vary, to the solid phase taught in Pieken et al., depending upon preference or the availability of useable derivatized oligonucleotides and would have had a reasonable expectation that the known methods would successfully perform their known and expected function of covalent binding for immobilization to a solid phase containing

carboxylated groups or derivatives thereof. One would have had an extremely reasonable expectation of success in using the cationic detergent reagents of Nikiforov et al. in the immobilization methods of Vary and/or Pieken et al. because Nikiforov et al. had already shown such reagents to be effective for oligonucleotide immobilization when mixed with oligonucleotides and one would have been motivated to have selected from known alternatives to perform the immobilization. With regard to Vary, as modified by Pieken et al., one of ordinary skill in the art would have reasonably expected a mixture of the oligonucleotide with the EDC as taught in Nikiforov et al., rather than stepwise addition as done in Vary, to perform successfully in immobilization to carboxylate groups on a sensor surface in view of the prior successful use of the mixture for immobilization. With regard to Pieken et al., nothing unobvious is seen in the substitution of one known reagent for another, that is detergent for salt, to obtain the expected predictable result of increasing hydrophobic conditions and increasing the reaction rate.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Husar et al. (Nucleosides, Nucleotides, & Nucleic Acids 20: 559, 2001) teach some results of the immobilization method as taught in Pieken et al. (US 7,427,678).

Chatterjee et al. (Biophys. Chem. 98: 313, 2002) teach micelles of cetyltrimethylammonium bromide (CTAB) and deoxyribonucleic acid.

Reddy et al. (US 5,648,213) teach conventional alternatives for binding oligonucleotides to solid supports (see e.g. col. 10).

Karlsson et al. (Anal. Biochem. 300: 132, 2002) contacted a sensor surface, having a carboxymethyl-modified dextran hydrogel thereon, with mixed micelles comprising octylglucoside and lipids, considered herein a low molecular weight organic molecule. The mixed micelles of the method of the reference delivered the lipids to the surface of the sensor and immobilized the lipids thereto, as well as to the immobilized rhodopsin protein, when the octylglucoside was washed from the micelles. Thus the micelles complexed with an immobilized protein and contacted the sensor surface. After use, the surface was washed, leaving the immobilized protein disassociated from the components of the mixed micelles for re-use. Proteins such as the exemplified rhodopsin carry many charges, both positive and negative.

Czerkinsky et al. (J. Immunol. Meth. 65: 109, 1983) teach the enzyme-linked immunospot assay for the determination of antibody-secreting cells. Cells, considered herein as vesicular structures, suspected of containing antibodies are applied to a solid phase having bound thereon a member of a specific binding pair, antigen, to bind target molecule, antibody, released from the cells. Different antigens are bound to different surfaces. Different antibodies are produced by different cells. The antibodies are bound to antigen on the solid phase surface, the cells are removed, and the bound antibodies are detected at discrete locations.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, SPE, can be contacted at (571) 272-0806.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun, Ph.D.
Examiner, Art Unit 1641
December 16, 2009

/Shafiqul Haq/
Primary Examiner, Art Unit 1641